Remarks

Upon entry of the amendments, claims 1, 3, 5-9, 11-14, 20-22, 27, 54-60, and 63-66 will be pending in the application. Claims 61 and 62 are cancelled, and clams 63-66 newly added. Support for the amendments to claims 1 and 60 appears at, e.g., page 8, lines 16-20. Support for new claims 63-66 appears in, e.g., original claim 20. No new matter has been added.

Rejection under 35 USC 112, first paragraph

Claims 1, 3, 5-9, 11-14, 20-22, 27, and 54-62 are rejected for overbreadth and for lack of written description. Claims 61 and 62 have been cancelled. The rejections are traversed to the extent they are applied to the claims as amended.

In maintaining the rejection for lack of written description, the Examiner states on page 3, last sentence:

> [A]bsent the ability to predict which of these polypeptides would function as claimed, and given the lack of data on regions critical for activity, for one of ordinary skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

Applicants respectfully disagree and submit that the amended claims satisfy the requirement for enablement and written description. Moreover, as is explained below, the specification does provide teachings of the regions of the GPIbα polypeptide that are important for activity.

The requirements for satisfying the written description requirement are set forth in MPEP 2163 (8th Ed., 2003):

> An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention.
>
> ***
>
> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

Claim 1, from which depends claims 3, 11-14, 20-22, 27 and 54-59, and claim 59 have been amended to specify that the recited glycoprotein Ibα polypeptide sequence includes an amino acid other than glycine at position 233 or an amino acid other than methionine at position 239 relative to the amino acid sequence of a wild-type GPIbα polypeptide. The claims additionally require that the first polypeptide comprises a polypeptide sequence with at least 85% homology to an extracellular portion of a glycoprotein Ibα polypeptide of SEQ ID NO:1, and that the first polypeptide binds a polypeptide selected from the group consisting of leukocyte integrin Mac-1 polypeptide, von Willebrand factor, thrombin and P-selectin.

The claimed invention is therefore claimed with reference to specific structural and functional requirements. The specification provides a detailed explanation of the correlation between these functions and structural characteristics. For example, the specification at page 8, lines 5-32 provides extensive teachings of those regions and amino acid residues of GPIbα that bind with higher affinity to von Willebrand factor and which are important for protein stability. Thus, the specification correlates a structure for the claimed invention.

With these teachings in the specifications the artisan can readily determine that Applicants were in possession of the invention at the time of filing the application.

The specification also provides detailed teachings for making (pages 7-20) and using (pages 20-28) the claimed polypeptides. Methods for detecting binding of a GPIbα protein to a ligand such as those recited in claim 1 are also well known in the art (see, e.g., Simon et al., J. Exp. Med. 192:193-204, 200, cited by Applicants at page 25, lines 30-32). Thus, one of ordinary skill in the art can readily practice the full scope of the invention now claimed using the teachings of the specification.

In view of the foregoing comments, Applicants request reconsideration and withdrawal of the rejection for lack of written description and enablement.

Rejections under 35 USC 103(a)

Claims 1, 3, 11-14, 20-22, 27, and 54-62 are rejected as a being unpatentable over Lopez et al., (Proc. Natl. Acad. Sci. USA, 84:5615-19, 1987; hereinafter, "Lopez") in view of U.S. Patent No. 6,277,975 (hereinafter, "the '975 patent"). Claims 61 and 62 are cancelled. The rejection is traversed to the extent it is applied to the claims as amended.

For an invention to be *prima facie* obvious, all of the imitations must be taught or suggested by the prior art. (MPEP 2143.03). Here, there is no teaching or suggestion in either reference of a polypeptide with the claimed GPIbα sequence. Claim 1, from which depends claims 3, 11-14, 20-22, 27 and 54-59, and claim 59 have been amended to specify that the recited glycoprotein Ibα polypeptide sequence includes an amino acid

other than glycine at position 233 or an amino acid other than methionine at position 239 relative to the amino acid sequence of a wild-type GPIbα polypeptide.

Lopez is cited for disclosing a GPIbα polypeptide with a wild-type sequence. However, there is no teaching or suggestion in Lopez of protein or fusion protein that includes the GPIbα polypeptide sequence now claimed. The '975 patent does not disclose any GPIbα polypeptide sequences. Therefore, the combination of Lopez and the '975 patent fail to produce the combination now claimed because neither reference teaches or suggests a fusion polypeptide that includes the claimed GPIbα polypeptide sequence.

Claims 1, 3, 5-9, 10-14, 20-22, 27 and 54-60 remain rejected as being unpatentable over Miura *et al.*, J. Biol. Chem., 275:7539-46, 2000 (hereinafter, "Miura") in view of the '975 patent. The rejection is traversed to the extent it is applied to the claims as amended.

In order to establish a case of obviousness by combining references there must be a suggestion or motivation for such a combination originating within the references themselves. The resulting combination must arrive at the claimed invention considered as a whole. The Federal Circuit has stated (In re Vaeck, 20 USPQ2d 1438, 1442, 1991):

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this [invention] should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art. Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure.

There is no suggestion or expectation of success in the combination of Miura and the '975 patent of a fusion polypeptide that includes a GPIba variant polypeptide

component, i.e., a GPIbα polypeptide portion that has an amino aid other than a methionine at position 233 or other than methionine at position 239 relative to the amino acid sequence of wild-type human GPIbα, and a portion of an immunoglobulin polypeptide.

While Miura describes GPIbα polypeptides with G233V and G239V mutations, it also teaches that "[t]he GPIbα mutants G233V and M239V cause platelet-type pseudo-von Willebrand disease" (see Abstract of Miura)." Miura lacks any other teaching that GPIbα mutants with these sequences would nevertheless be a useful as a therapeutic agent.

The Examiner has relied on the '975 patent to provide a motivation for making the claimed polypeptide. The Examiner pointed in the January 30, 2003 Office Action at page 9 to the desirable physiological properties of a fusion polypeptide containing an immunoglobulin moiety:

> The '975 patent further teaches that Fc portion of native or mutated immunoglobulin sequences for longer half life or reduced immunogenicity (see column 10 lines 37-40 in particular. Finally, the '975 patent teaches pharmaceutical compositions comprising P-selectin ligand proteins (column 4, lines 48-50) in particular.
>
> It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the Calmodulin peptide taught by Miura et al. with the Fc portion of a human IgGg1 taught by the '975 patent.
>
> One of ordinary skill in the art at the time the invention was made would have been motivated to do so because Fc portion of native or mutated immunoglobulin sequences conferring desirable qualities such as longer half-life or reduced immunogenicity as taught by the '972 patent.

However, to the extent this provides motivation for making a fusion protein, it only would provide motivation for making a fusion protein that would be used as a

therapeutic agent. There is no teaching or suggestion in Miura that its variant GPIbα polypeptides could be used to treat a disease or condition. Therefore, the artisan would have no motivation for making a fusion protein by combining the variant GPIbα disclosed in Miura with the immunoglobulin polypeptides disclosed in the '975 patent. Alternatively stated, the artisan would have no motivation to prolong the half life or lessen the immunogenicity of a variant GPIbα polypeptide for which Miura itself gives no reason to think has a therapeutic use. Moreover, because the variant polypeptides are associated with a disease, there is no expectation that combining the variant GPIbα polypeptides with the '975 immunoglobulin sequences would be successful for making a therapeutic polypeptide.

As Applicants' explained previously, there is also no motivation or expectation of success in replacing the calmodulin moiety in the GPIbα calmodulin fusion protein described in Miura with an immunoglobulin moiety described in the '975 patent. Miura reports that the calmodulin is present to facilitate purification of this fusion protein on a phenothiazine derivative W-7 agarose column. One of ordinary skill in the art would not replace the calmodulin moiety in the Miura fusion protein with an immunoglobulin moiety because such a substitution would render the fusion protein unusable for the purpose Miura requires, i.e., capture on a phenothiazine derivative W-7 agarose column.

Claims 61-62 are rejected being unpatentable over Miura in view of the '975 patent and further in view of U.S. Patent No. 5,340,727 (hereinafter, "the '727 patent"). Claims 61 and 62 have been cancelled. Therefore, the rejection as applied to these claims is moot.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejections for obviousness.

Applicants submit that the application is in condition for allowance, and such action is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

A petition for extension of time and request for continued examination accompany this response. The Commissioner is authorized to charge payment of any additional fees required in connection with the papers transmitted herewith, or credit any overpayment of same, to Deposit Account No. 50-0311 (Reference No. 22058-503).

Respectfully submitted,

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